REMARKS

Reconsideration is requested.

Claims 1-7, 13 and 14 are pending.

Claim 1 has been revised, without prejudice, to indicate that the interaction is specific in that the compound does not react with the majority of molecules present in the mixture. Basis for this amendment can be found on page 5, lines 7-9 and on page 11, line 29-32 of the originally-filed application (WO2004/025243). Basis for the revision to claim 14 can be found, for example, on page 14, lines 26-28 of the specification. That this is prior to the second chromatographic step can be derived from several passages in the application, such as for example on page 14, lines 28-36 and Example 1.6.

The objection to claim 1 is obviated by the above amendments. Withdrawal of the objection is requested.

The Section 112, first paragraph "written description", rejection of claims 1-7, 13 and 14 is obviated by the above amendments. The objected-to phrase has been deleted. Withdrawal of the Section 112, first paragraph, rejection is requested.

The Section 112, second paragraph, rejection of claims 5 and 14 is traversed. Reconsideration and withdrawal of the rejection are requested in view of the above and the following. The recitation objected-to in claim 5 has been deleted above, without prejudice, to advance prosecution.

Similarly, claim 14 has been revised, without prejudice, to obviate the rejection. The applicants note that the idea of avoiding elution of multiple overlapping peaks into

the same fraction is not just important for random peak discrimination, but for being able to distinguish the peak of the altered complex (which has a different elution time than the unaltered complex). Thus, pooling will not be done with 'neighbouring' fractions, as the altered complex will typically shift to just in front or just behind the fraction it was in, in the first separation. See for example, the peak in front of fraction 14 in Figure 3B. Applicants believe this is reflected by the current claim language, as for example, table 1 show that a plurality of the fractions of the primary run having distinct elution times (e.g. 1-6-11-16-21 or 4-9-14-19-24) are pooled into a plurality of pooled fractions (A-E in Table 1).

The claims are submitted to be definite and withdrawal of the Section 112, second paragraph, rejection is requested.

To the extent not obviated by the above amendments, the Section 103 rejection of claims 1-7 over Creighton ("Proteins: Structures and Molecular Properties" Second Edition, W.H. Freeman and Company, New York, 1993, pages 10-20 and 31-41) in view of Aebersold (U.S. Patent No. 6,670,194), is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing remarks.

The cited art fails to teach or suggest the claimed invention, especially with regard to the interaction with a 'specific' interaction partner.

The claims specify that when a compound is added to a complex mixture of molecules, the compound interacts with a specific interaction partner, but does not interact with the majority of the molecules in the mixture. This is an important concept of the claimed invention. The activity of drugs is due to the specific interaction with

molecules influencing their biological activity, and a drug will typically target only one or a limited number of molecules (e.g. a particular protein class) – see e.g. page 7 of the application, lines 20-28, as originally filed.

The isolation of specific molecules is not the same as protein quantification of a sample by reaction with particular amino acids – see the following passage from page 1, lines 26-32 of the originally-filed specification:

> "For example, methods currently described in the art provide chemically reactive compounds that can be reacted with a protein mixture to label many proteins in that mixture in a non-specific, or non-directed, manner providing only a quantitative analysis of proteins (Link et al. (1999) Nat. Biotechnol. 17,676-682, Gygi et al. (1999) Nat. Biotechnol. 17,994-999). Such methods teach that there are many chemically reactive amino acid residues within a protein which can be conjugated to chemical probes, whereby the resulting protein complexes can be subsequently quantified to yield an indication of protein abundance."

The above claims specify that the compound does not react with the majority of molecules.

Neither Creighton nor Aebersold et al., alone or in combination, teach or suggest a lack of reaction with the majority of molecules. Creighton is silent on this topic, while it is specified in Aebersold et al. that the affinity labeled reagent is designed to react with peptides of each protein in a mixture in order to allow protein quantitation and identification for the whole sample (e.g. column 3, lines 9-15; column 5, lines 55-60; column 15, lines 54-57). To achieve this, the reagent should be able to react with peptides derived from each protein. Proteins that do not react with a particular reagent

may still be targeted by including reactivity to other groups, as described in column 16, lines 45-52 of the Aebersold patent:

> "The method can be extended to include reactivity toward other functional groups. A small percentage of proteins (8% for *S. cerevisiae*) contain no cysteinyl residues and are therefore missed by analysis using reagents with sulfhydryl group specificity (i.e., thiol group specificity). Affinity tagged reagents with specificities toward functional groups other than sulfhydryl groups will also make cysteine-free proteins susceptible to analysis."

On of ordinary skill will appreciate the implication in the art that the reagent reacts with 92% of the proteins present in the mixture, i.e. with the majority of the molecules, which would be contrary to the claims of the present application. Moreover, the Aebersold patent teaches that an advantage and desirability to increase this coverage because otherwise the proteins are 'missed by analysis'. This is not only different from what is taught in the present application, but a clear teaching away of the presently claimed invention.

Creighton fails to cure these deficiencies. Creighton is silent as to the amount of molecules with which interaction is desired – only one protein is analysed, and the compound interacts with the protein. Moreover, Creighton, like Aebersold et al., relates to modification of particular amino acids, and all cysteine-containing peptides of the protein are identified. The combination of Creighton and Aebersold et al. thus at best would have been expected to result in a method in which ideally each protein reacts with a given compound, so that at least one peptide representative of the protein is labeled. In each case, was no teaching or suggestion in the cited art that it would have

been beneficial to use a compound that only interacts with a minority of the molecules in a mixture. One of ordinary skill in the art would not have predictably made the claimed invention wherein only reaction with specific interaction partners of the compound is envisaged, while no reaction occurs with the majority of the molecules in a given mixture.

The claimed invention would not have been obvious in view of the cited combination of art and withdrawal of the Section 103 rejection over same is requested.

The Section 103 rejection of claim 13 over Creighton and Aebersold "as evidenced by" Sahasrabudhe (U.S. Patent No. 5,705,351) or Chang (U.S. Patent No. 5,474,780); and the Section 103 rejection of claim 14 over Creighton, Aebersold and GE Healthcare ("Fraction Collectors: Frac-950 and Frac-920", Data File 18-1153-57 AD (May 2001), retrieved from http://www1.gelifesciences.com on 4/8/09), are traversed. Reconsideration and withdrawal of the rejections are requested in view of the above. The additionally rejected dependent claims are submitted to be patentable over the combination of art for the reasons noted above with regard to claim 1, from which the rejected claims depend, as the additionally cited art fails to cure the above-noted deficiencies.

Withdrawal of the Section 103 rejections are requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned, preferably by telephone, in the event anything further is required.

Respectfully submitted,

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